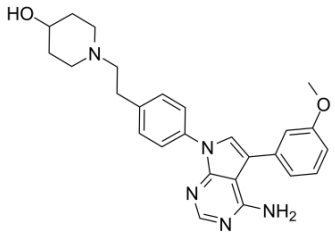
CGP77675

Cat. No.:	HY-W062835
CAS No.:	234772-64-6
Molecular Formula:	$C_{26}H_{29}N_5O_2$
Molecular Weight:	443.54
Target:	Src
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	-20°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



BIOLOGICAL ACTIVITY

Description

CGP77675 is a potent inhibitor of Src family kinases. CGP77675 inhibits Src, EGFR, KDR, v-Abl, and Lck with IC_{50}s of 0.02, 0.15, 1.0, 0.31, and 0.29 μM, respectively. Anticancer activity[1].

IC_{50} & Target

IC50: 0.02 μM (Src), 0.15 μM (EGFR), 1.0 μM (KDR), 0.31 μM (v-Abl), 0.29 μM (Lck)[1]

In Vitro

CGP77675 inhibits phosphorylation of peptide substrates and autophosphorylation of purified Src (IC_{50}s of 5-20 and 40 nM, respectively) [1].

CGP77675 dose dependently inhibits phosphorylation of poly-Glu-Tyr with an IC_{50} value of 5.5 nM, and of the optimal Src substrate (OSS) peptide with an IC_{50} value of 16.7 nM. These IC_{50} values are similar to the value obtained with chicken Src (20 nM)[1].

CGP77675 inhibits the parathyroid hormone-induced bone resorption in rat fetal long bone cultures with an IC_{50} of 0.8 μM[1].

CGP77675 (0.04-10 μM; 2 hours) potently inhibits tyrosine phosphorylation of the Src substrates Fak and paxillin, but has much less effect on Src (IC_{50} values 0.2, 0.5, and 5.7μM) in IC8.1 cells[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	MC3T3-E1 cells
Concentration:	0.2, 1, and 5 μM
Incubation Time:	3 days
Result:	Did not influence cell viability for up to 3 days of treatment.

Western Blot Analysis[1]

Cell Line:	Src-overexpressing IC8.1 cells
Concentration:	0.04, 0.2, 1, 5, and 10 μM
Incubation Time:	2 hours
Result:	Dose dependently inhibited phosphorylation of Fak and paxillin, but not of Src.

In Vivo

CGP77675 (1, 5, and 25 mg/kg; injected s.c.; twice a day) inhibits IL-1β-induced hypercalcemia in Mice[1].

CGP77675 (10 and 50 mg/kg; administered orally; twice a day for 6 weeks) partially prevents bone loss and rescues bone microarchitectural features in young ovx rats[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male mice (Tif:MAGf; Novartis Animal Farm) of 25-30 g body[1]
Dosage:	1, 5, and 25 mg/kg
Administration:	Injected s.c.; twice a day
Result:	Prevented IL-1β-induced hypercalcemia in mice without affecting serum amyloid protein levels.

Animal Model:	Eight-week-old (175-209 g) female rats of the Sprague-Dawley-derived strain Tif:RAlf[1]
Dosage:	10 and 50 mg/kg
Administration:	Administered orally; twice a day for 6 weeks
Result:	Partly prevented bone loss.

REFERENCES

[1]. Missbach M, et al. A novel inhibitor of the tyrosine kinase Src suppresses phosphorylation of its major cellularsubstrates and reduces bone resorption in vitro and in rodent models in vivo. Bone. 1999 May;24(5):437-49.

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